BACKGROUNDER

Veterinary Services

United States Department of Agriculture

Animal and Plant Health Inspection Service

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Transmissible Spongiform Encephalopathies (TSE)

TSE's are rare forms of progressive neurodegenerative disorders that affect both humans and animals and are caused by similar uncharacterized agents that generally produce spongiform changes in the brain. Specific examples of TSE's include: scrapie, which affects sheep and goats; bovine spongiform encephalopathy (BSE), which affects cattle; transmissible mink encephalopathy; feline spongiform encephalopathy; chronic wasting disease (CWD) of mule deer, white-tailed deer, black-tailed deer, and elk; and in humans, kuru, Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, fatal familial insomnia, and variant Creutzfeldt-Jakob disease (vCJD).

Diagnosis: TSE's are insidious degenerative diseases of the central nervous system. Historically, the diagnosis of TSE's has been based on the occurrence of clinical signs of the disease, which was confirmed only by postmortem examination of brain tissue. More recently, identification of abnormal prion protein, PrP^{res}, by various techniques has improved our ability to make a disease diagnosis.

Laboratory Testing: A characteristic feature of all TSE's is the lack of a measurable host immune response to the agent meaning that there are no antibodies produced. No conventional serologic test can be used to identify infected animals. Scientists usually diagnose TSE diseases in the laboratory by histopathologic examination of the brain followed by one or more supplemental tests. A description of these tests is attached.

Scrapie: Scrapie was first diagnosed in the United States in 1947. Control programs have been in place since 1952. The latest program went into effect in 1992. It involves a Flock Certification Program and interstate movement regulations that place restrictions on the movement of sheep and goats from infected and source scrapie flocks. The intent of the certification program is to monitor flocks over a period of 5 years or more and identify flocks that have not displayed evidence of scrapie. Flocks are inspected yearly for compliance with the certification program standards. The older the flock's status date the lower the risk of that flock having scrapie. APHIS has proposed a rule to strengthen the regulatory program by (1) requiring the identification of mature sheep and goats in interstate commerce, (2) restricting the interstate movement of sheep and goats from the States that do not have effective scrapie control programs, and (3) providing indemnity for scrapie-positive and high-risk animals.

CWD: CWD is a TSE of deer and elk. Species that have been affected include mule deer, white-tailed deer, black-tailed deer, and elk. The disease occurs in free-ranging mule deer and elk in northeastern Colorado and southeastern Wyoming. In 1997, CWD was found in farmed elk herds in South Dakota. Subsequently, CWD was diagnosed in farmed elk in Nebraska, Oklahoma, Colorado, and Montana. APHIS, in cooperation with the States and industry, is currently developing a CWD program for controlling and eliminating this disease in farmed cervids. APHIS is also cooperating with State wildlife agencies in Colorado and Wyoming where the disease occurs endemically in free-ranging cervids and also with other wildlife agencies that are conducting surveillance in nonendemic States to clearly define the distribution of CWD in free-ranging cervids.

BSE: BSE is a TSE of cattle, which was first diagnosed in 1986 in Great Britain. Epidemiological data suggest that BSE in Great Britain is a common source epidemic involving animal feed containing contaminated meat-and-bone meal as a protein source. There is no evidence that BSE spreads horizontally, i.e., by contact between unrelated adult cattle or from cattle to other species. BSE has not been identified in native cattle outside of Europe, and more than 95 percent of all BSE cases identified in the world have been in the United Kingdom. BSE has not been diagnosed in the United States, and USDA has worked proactively to keep it that way. The United States has one of the most aggressive BSE surveillance programs in the world. Since 1989, APHIS has prohibited the importation of live ruminants from countries where BSE is known to exist in native cattle. Other products derived from ruminants, such as fetal bovine serum, bonemeal, meat-and-bone meal, bloodmeal, offal, fats, and glands, are also prohibited entry, except under special conditions with a USDA permit for scientific or research purposes.

TME: There is no official USDA program for TME. We continue to monitor for reoccurrence of TME disease. The last known case of TME occurred in the United States in 1985. There were other outbreaks prior to 1964.

Testing Methods for TSE's

Histopathology: Bilaterally symmetrical degenerative changes are usually seen in the gray matter of the brain stem. These changes are characterized by vacuolation or microcavitation of nerve cells in the brain stem nuclei. The neural perikarya and axons of certain brain stem nuclei contain intracytoplasmic vacuoles of various sizes, giving the impression of a spongy brain. Hypertrophy of astrocytes (astrocytosis) often accompanies the vacuolation.

Electron Microscopy: A TSE diagnosis may also be made when scrapie-associated fibrils (SAF) using negative stain electron microscopy are detected.

Supplemental tests: Supplemental tests are available to enhance the diagnostic capabilities for TSE's. Research shows the partially protease-resistant form of the prion protein (PrP^{res}) is found in the brain of TSE-infected animals. Two tests that have been used routinely to detect PrP^{res} in animals showing clinical signs of a TSE are immunohistochemistry and a Western-blot technique. In the past, if the brain tissue was not harvested shortly after the animal's death, autolysis might make it very difficult to confirm a diagnosis by histopathology, but these tests permit a diagnosis of a TSE based on finding PrP^{res} even if the brain has been frozen or if autolysis has occurred.

Last year, the European Commission published a preliminary report on the evaluation of four companies' tests for the diagnosis of TSE in cattle brain samples. These included a modified Western-blot test developed by Prionics A.G. of Switzerland; a chemiluminescent ELISA test using a polyclonal antiPrP antibody for detection developed by Enfer Technology, Ltd., of Ireland; a sandwich immunoassy for PrP^{res} developed by Commissariat a l'Energie Atomique (CEA) of France; and a two-site noncompetitive immunometric procedure using monoclonal antibodies and DELFIA technology to generate a signal developed by E. G. & G. Wallace, Ltd., of the United Kingdom. The Prionics test is currently being used in Switzerland to test "fallen stock." Other countries, such as Germany and France, are going to start using the Prionics test or one of the other three tests to increase surveillance for BSE in cattle.

A number of tests have been proposed and are in the initial process of being validated for the preclinical diagnosis of TSE's in sheep. These include 1) immunohistochemistry testing of eyelid associated lymphoid tissue and tonsil biopsies, 2) use of capillary electrophoresis and fluorescent labeled peptides to detect PrP^{res} in the blood of animals infected with a TSE, and 3) improved Western-blotting techniques with very good sensitivity to detect PrP^{res} in blood, cerebrospinal fluid, or small pieces of biopsied tissues.

Agent Isolation: As the agents that cause TSE's have not been fully characterized or isolated, one method used to detect infectivity in an animal is to inoculate laboratory animals with brain material from the affected animal and monitor them for evidence of disease. This method may take more than 2 years to produce results; hence, it is not practical for routine testing. The most common animal used for this type of bioassay is the mouse. Another problem with the mouse bioassay method when testing cattle or sheep samples is that the species barrier may prevent detection of low levels of infectivity.